

REMARKS

Favorable consideration and allowance are respectfully requested for claims 1 and 3-67 in view of the following remarks. Rejoinder of the withdrawn claims is respectfully requested, to the extent applicable.

35 U.S.C. § 112, first paragraph

The rejection of claims 1 and 3-67 as allegedly lacking enablement is respectfully traversed.

Enablement is satisfied where the specification describes the claimed subject matter in such a way as to enable a person skilled in the art to which it pertains to use the invention. Thus, enablement is judged in view of the combined teachings of the specification and the knowledge of one skilled in the art.

The Office Action does not explain why a person skilled in the art would be unable to make or use salts of any of the pharmaceutically active ingredients embraced by the claim, nor does the Office Action give any example of a pharmaceutically active agent embraced by the claim with which a person of ordinary skill in the art would be unable to practice the invention. Again, applicants point out that because the phenomenon of the invention does not depend on the particular pharmaceutical activity of the active ingredient, the fact that the claim embraces agents with a broad variety of pharmaceutical activities is irrelevant. Salt formation is not unpredictable, and the teachings and examples of the specification are sufficient to demonstrate the effectiveness of the claimed invention over the entire range of claimed salt-forming pharmaceutically active agents.

The U.S. Court of Customs and Patent Appeals has stated that “The first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance.” *In re Marzocchi*, 169 USPQ 367 , 369 (CCPA 1971). The court also added that “it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or

accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.” *In re Marzocchi*, 169 USPQ 367 , 370 (CCPA 1971). The present record includes no statement or other explanation as to why the truth of the accuracy of statements in the disclosure should be doubted. The law does not require a separate showing of functionality for each and every drug encompassed by a claim.

The most recent Office Action asserts that the rejection is based on a belief that the Applicants lacked actual knowledge of the solubility properties of all possible active agents encompassed by the claims. In support of this position, the Office Action points to an alleged lack of “evidence on the record that the applicant had actual knowledge of the solubility properties of all possible active agents” (emphasis in original). This is a heightened standard for enablement and is not supported by the patent laws or even the MPEP. The law is clear that enablement does not require an example for all claimed embodiments.

As indicated in the MPEP at § 2164.08: “the scope of enablement must only bear a ‘reasonable correlation’ to the scope of the claims.” See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Section 2164.02 of the MPEP addresses the relationship between examples and enablement, stating:

Compliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed.

....

The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski*, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970).

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Lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped

art. But because only an enabling disclosure is required, *applicant need not describe all actual embodiments*. (emphasis added)

Thus, the law is clear that enablement does not require the every claimed embodiment be provided with an example. Indeed enablement may be satisfied without any working examples.

In the present instance, the scope of the claims is commensurate with the description provided in the specification. The examples provided in the specification and in the declaration of Dr. Bartholomaeus represent preferred embodiments which show that the release of an active substance may be modified using at least two different salts of the same active substance having a defined minimum difference in water solubility. These examples are, however, merely representative of the claimed invention and do not limit the general scope thereof.

The nature of the active substance as such is not relevant for the inventive modification of the release profile, as long as they are salts which fulfill the requirement with respect to solubility. This is the scope of the present applicant's discovery. The breadth of this discovery justifies the breadth of the claims presently under consideration. There is nothing in the patent laws that limits the scope of the allowable claim to the particular examples of tramadol and promethazine. The inventive modification of the release profile of the active substance is achieved by the same underlying principle, *i.e.* the selection of salts in such a way that their water solubility differs by at least a factor of 2. Consequently, salts of any active substance having the defined minimum difference of water solubility may be used according to the presently claimed invention to modify the release of said active substance.

Accordingly, the full scope of the present claims is justified by the scope of the inventive discovery, and the claims are fully enabled. Reconsideration and withdrawal of this rejection are respectfully requested.

35 U.S.C. § 103

The rejection of claims 1-9, 11, 12, 15, 17, 18, 21, 30-32, 55-58 and 62-67 as obvious over Oshlack et al., WO 99/01111, in view of Sackler, U.S. 5,478,577, is also respectfully traversed.

There is nothing in the cited prior art which teaches or suggests using a mixture of two different salts of the same pharmaceutically active ingredient having different solubilities as is presently claimed.

Situations involving mixtures of two different pharmaceutically active agents are very different from mixtures of two different salts of the same active agent as claimed in the present invention. The record is devoid of any example of a mixture of different salts of the same active agent, and with good reason. A person of skill in the art would have no reason to expect that a mixture of two different salts of the same active ingredient would provide any benefit beyond either of the salts alone. There is nothing in the present record which would lead a person of skill in the art to expect any advantage from using a mixture of two materials over using a single material when there is only one active ingredient present in the mixture. The formation of a mixture of two different salts of the same active ingredient is unquestionably more troublesome and inconvenient than the provision of a single salt.

All that the prior art would lead a person of ordinary skill in the art to expect would be that such a mixture of salts of the same active ingredient would have the same effect as a single salt of the active ingredient. Thus, the prior art gives a person of ordinary skill in the art no reason or motivation to form such a mixture of salts of the same active ingredient. Accordingly, it cannot be fairly be said to be obvious for a person of ordinary skill to incur the trouble and inconvenience of forming such a mixture for no reason.

Not only does the cited art fail to teach or suggest the use of a mixture of different salts of the same active ingredient, the present record provides no teaching or other suggestion to use a mixture of salts having solubilities which differ from one another by at least a factor of two.

As set forth in § 706.02(j) of the Manual of Patent Examining Procedure (MPEP), Patent and Trademark Office, U.S. Department of Commerce, (8th ed. Rev. 3, August, 2005), for a proper obviousness rejection:

First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

On the present record, there is no showing of why a person of skill in the art would be motivated to try to combine the references as proposed in the Office Action. Moreover, even assuming one of skill in the art were, for some reason, inclined to try to combine the references, there is nothing that would cause the person to try to modify the teachings there as necessary to meet the present claims. In particular, there is nothing to cause one of skill in the art to think they might achieve any benefit by combining different salts of the *same active ingredient*. As a result, not only does the proposed combination fail to teach or suggest the claim limitations, but there is nothing that would provide one of skill in the art with any expectation of success in achieving a useful result by combining different salts of the same active ingredient. In view of the foregoing, the present record fails to establish a *prima facie* case of obviousness and the obviousness rejection cannot be properly maintained.

As indicated previously, the Declaration of Dr. Bartholomaeus shows test results comparing the release profile of: (i) tramadol hydrochloride, (ii) tramadol saccharinate and (iii) a mixture of tramadol hydrochloride and tramadol saccharinate. The results show that the drug release profile may be adjusted by having different salts of the same active substance in a single formulation. This is an unpredicted and unexpected result, so that even assuming, *arguendo*, that the cited combination of references amounted to a *prima facie* showing of obviousness, in view of the unexpected results, the claimed invention should be determined nonobvious.

Accordingly, reconsideration and withdrawal of the obviousness rejection are respectfully requested.

CONCLUSION

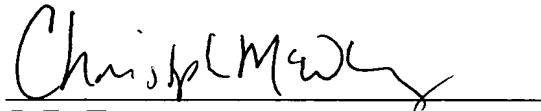
In view of the foregoing remarks, the application is respectfully submitted to be in condition for allowance, and prompt, favorable action thereon is earnestly solicited.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323 (Docket No. 029310.50986).

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Respectfully submitted,



J. D. Evans

Registration No. 26,269

Christopher T. McWhinney

Registration No. 42,875

CROWELL & MORING LLP
Intellectual Property Group
P.O. Box 14300
Washington, DC 20044-4300
Telephone No.: (202) 624-2500
Facsimile No.: (202) 628-8844
JDE:CTM:mdm (2857856)